

## P. ENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
 US Department of Commerce  
 United States Patent and Trademark  
 Office, PCT  
 2011 South Clark Place Room  
 CP2/5C24  
 Arlington, VA 22202  
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

<b>Date of mailing</b> (day/month/year) 11 May 2001 (11.05.01)	
<b>International application No.</b> PCT/US00/24437	<b>Applicant's or agent's file reference</b> PCT 20194
<b>International filing date</b> (day/month/year) 06 September 2000 (06.09.00)	<b>Priority date</b> (day/month/year) 10 September 1999 (10.09.99)
<b>Applicant</b> EL-SHERBEINI, Mohammed et al	

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

29 March 2001 (29.03.01)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<b>The International Bureau of WIPO</b> 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Olivia TEFY Telephone No.: (41-22) 338.83.38
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## PATENT COOPERATION TREATY

## PCT

REC'D 12 NOV 2002

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PCT 20194	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/24437	International filing date (day/month/year) 06 September 2000 (06.09.2000)	Priority date (day/month/year) 10 September 1999 (10.09.1999)
International Patent Classification (IPC) or national classification and IPC IPC(7): C07H 21/02, 21/04; G01N 33/53; C12N 15/00, 15/09, 15/63, 15/70, 15/74, 9/00, 1/20, 1/14, 1/16, 1/18, and US Cl.: 536/23.1, 23.2; 435/320.1, 183, 7.71, 252.3, 254.11, 419, 325		
Applicant MERCK & CO., INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.  
☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:
  - I ☒ Basis of the report
  - II ☐ Priority
  - III ☒ Non-establishment of report with regard to novelty, inventive step and industrial applicability
  - IV ☒ Lack of unity of invention
  - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
  - VI ☐ Certain documents cited
  - VII ☒ Certain defects in the international application
  - VIII ☒ Certain observations on the international application

Date of submission of the demand 29 March 2001 (29.03.2001)	Date of completion of this report 24 September 2002 (24.09.2002)
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer <i>Kathleen M Kerr</i> Kathleen M Kerr Telephone No. (703) 308-0196

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/24437

## I. Basis of the report

## 1. With regard to the elements of the international application:\*

- ☐ the international application as originally filed.
- ☒ the description:  
pages 1-24 as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_.
- ☒ the claims:  
pages 25-28, as originally filed  
pages NONE, as amended (together with any statement) under Article 19  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_.
- ☒ the drawings:  
pages 1-4, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_.
- ☒ the sequence listing part of the description:  
pages NONE, as originally filed  
pages NONE, filed with the demand  
pages 1-3, filed with the letter of 30 October 2000 (30.10.2000).

## 2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

## 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages NONE
- ☐ the claims, Nos. NONE
- ☐ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/24437

## III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 12-14

because:

- ☐ the said international application, or the said claim Nos. \_\_\_\_\_ relate to the following subject matter which does not require international preliminary examination (*specify*):

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_ are so unclear that no meaningful opinion could be formed (*specify*):

- ☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported by the description that no meaningful opinion could be formed.

- ☒ no international search report has been established for said claims Nos. 12-14

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
- ☐ the computer readable form has not been furnished or does not comply with the standard.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/24437

**IV. Lack of unity of invention**

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☒ restricted the claims.  
☐ paid additional fees.  
☐ paid additional fees under protest.  
☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention is accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.  
☒ not complied with for the following reasons:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1-8, drawn to polynucleotides encoding MurF, vectors, host cells, methods of making MurF polypeptides using polynucleotides, and MurF polypeptides.

Group II, claims 9-11, drawn to methods of determining inhibitors of MurF polypeptides using host cells containing polynucleotides encoding said polypeptides.

Group III, claims 12-13, drawn to inhibitors of MurF polypeptides and compositions thereof.

Group IV, claim 14, drawn to methods of treatment using inhibitors of MurF polypeptides.

Group V, claims 15-17, drawn to methods of determining inhibitors of MurF polypeptides using said polypeptides.

The inventions listed as Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons.

The special technical feature of Group I is MurF polypeptides which are encoded by the claimed polynucleotides which are contained in the vectors and host cells. Claim 7 is included as a first method of making the special technical feature, MurF polypeptides; claim 7 is also a first method of using the polynucleotides.

Group II is an additional method of using the polynucleotides and/or host cells. As such, said method need not be grouped with the first method of using in Group I.

Group III, while being related to the special technical feature of MurF polypeptides in that the compounds inhibit said polypeptides, are not integrally related to the special technical feature having different structural and functional compositions.

Group IV, while being related to the special technical feature of MurF polypeptides in that the compounds used in the methods of treatment inhibit said polypeptides, are not methods of using the special technical feature itself.

Group V, is an additional method of using the polypeptides. As such, said method need not be grouped with the first method of using in Group I.

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☐ all parts.  
☒ the parts relating to claims Nos. 1-8

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.  
PCT/US00/24437**V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. STATEMENT**

Novelty (N)	Claims <u>6-8</u>	YES
	Claims <u>1-5</u>	NO
Inventive Step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-8</u>	NO
Industrial Applicability (IA)	Claims <u>1-8</u>	YES
	Claims <u>NONE</u>	NO

**2. CITATIONS AND EXPLANATIONS**

Claims 1-5 lack novelty under PCT Article 33(2) as being anticipated by Dewar et al. as evidenced by Sanschagrin et al. and Ikeda et al. The instant claims are drawn to polynucleotides and vectors comprising DNA encoding the murF polypeptide, disclosed as SEQ ID NO:2. Dewar et al. teach the DNA of the entire *fts-mur* locus in *Pseudomonas aeruginosa* PAO1 (see Abstract and Figure 7)). While Dewar et al. do not specifically cite the murF gene within the DNA disclosed, the DNA disclosed by Dewar et al. inherently comprises the murF gene. The locus taught by Dewar et al. is a 110-kb portion with approximately 52 kb on either side of *ftsW-murG-murC* (see Figure 7). This locus is "remarkably similar to those found in the genomes of *E. coli*, *B. subtilis*, *H. influenzae*, and other bacterial species" as taught by Sanschagrin et al.; and Ikeda et al. teach the locus in *E. coli* with murF adjacent to *ftsW-murG-murC* within 17kb (see Figure 6 and page 185). Thus, the 110-kb piece of DNA taught by Dewar et al. inherently comprises the murF gene; as such, the murF gene is taught in its isolated form.

Claims 6-8 lack an inventive step under PCT Article 33(3) as being obvious over Dewar et al. as evidenced by Sanschagrin et al. and Ikeda et al. Dewar et al., Sanschagrin et al., and Ikeda et al. teach as described above. These references do not teach the expression of the encoded proteins of the mur locus.

It would have been obvious to express the murF polypeptide since the murF polypeptide is described for *E. coli* and other bacterial systems (see Ikeda et al.).

Claims 1-8 meet the criteria set out in PCT Article 33(4), because the nucleotides and polypeptides of MurF from *Pseudomonas aeruginosa* have industrial applicability due to the pathogenic nature of *Pseudomonas aeruginosa* and such products would foreseeably facilitate specific antibacterial therapeutics.

□

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/24437

**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:

The description is objected to as containing the following defect(s) under PCT Rule 66.2(a)(iii) in the form or contents thereof: on page 20, lines 18-19, there are blanks where deposit information should be. Appropriate correction is required.

Claims 2-3 are objected to under PCT Rule 66.2(a)(iii) as containing the following defect(s) in the form or contents thereof: Claims 2 and 3 do not limit the subject matter of the parent claim. In Claim 2, natural, non-natural, and modified nucleotides encompass *all* nucleotides. In Claim 3, natural and non-natural linkages encompass *all* linkages.

Claim 7 is objected to under PCT Rule 66.2(a)(iii) as containing the following defect(s) in the form or contents thereof: in item (b), line 1, the term "under" should be deleted for clarity of the claim language.



## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/24437

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claims 1-3, 5-7, and 15-17 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claim 1 is indefinite for the following reason(s):

In Claim 1, item (d), the term "stringent conditions" is not defined in the instant specification such that the metes and bounds of the invention are clear;

In Claim 1, item (e), the phrase "being specific for *murF* gene" is not defined in the instant specification such that the metes and bounds of the invention are clear; and

In Claim 15, item (ii) the term "functional derivative" is not defined in the instant specification such that the metes and bounds of the invention are clear.

The description is objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 5 because it fails to contain an adequate written description of naturally occurring mutants or polymorphic variants of polynucleotides which encode SEQ ID NO:2. The description is inadequate because the structure of said variants cannot be reasonably predicted based on the disclosure.

Claims 1-3, 5-9, 11, 15, and 17 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because practice of the claimed invention is not adequately described in writing, as required under PCT Rule 5.1(a)(iii), for the reasons set forth in the immediately preceding paragraph.

The description is objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 5 because it fails to contain an adequate written description of:

-polynucleotides which hybridize to polynucleotides which encodes SEQ ID NO:2 but which do not encode an ATP-dependent amino acid ligase like the *murF* gene product;

-polynucleotides comprising at least 25 nucleotides specific for SEQ ID NO:1 but which do not encode an ATP-dependent amino acid ligase like the *murF* gene product; and

-polypeptides that are "functional derivatives" of SEQ ID NO:2 but which are not ATP-dependent amino acid ligase like the *murF* gene product.

The description is inadequate because the specification describes polypeptides, or polynucleotides encoding said polypeptides, which polypeptides are related to the *murF* gene product by virtue of structural *and* functional characteristics.

Claims 1-3, 5-9, 11, 15, and 17 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because practice of the claimed invention is not adequately described in writing, as required under PCT Rule 5.1(a)(iii), for the reasons set forth in the immediately preceding paragraph.

## SEQUENCE LISTING

&lt;110&gt; Merck &amp; Co., Inc.

<120> MURF GENE AND ENZYME OF PSEUDOMONAS  
AERUGINOSA

&lt;130&gt; 20194

&lt;150&gt; 60/153,293

&lt;151&gt; 2000-09-10

&lt;160&gt; 4

&lt;170&gt; FastSEQ for Windows Version 4.0

&lt;210&gt; 1

&lt;211&gt; 1449

&lt;212&gt; DNA

&lt;213&gt; Pseudomonas aeruginosa

&lt;400&gt; 1

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&lt;211&gt; 451

&lt;212&gt; PRT

&lt;213&gt; Pseudomonas aeruginosa

&lt;400&gt; 2

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27

REPLACED BY  
ART 34 AMDT

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	225					230					235					240
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&lt;220&gt;

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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/24437

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : Please See Extra Sheet.

US CL : 536/23.1, 23.2: 435/320.1, 183, 7.71, 252.3, 254.11, 419, 325

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.1, 23.2: 435/320.1, 183, 7.71, 252.3, 254.11, 419, 325

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAPLUS, BIOSIS, GenEmbl, Geneseq, EST, PIR62, SwissProt, SptrEmbl

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P ---	Database GenBank, US National Library of Medicine, (Bethesda, MD, USA), No. 9950633, STOVER et al. 'Pseudomonas aeruginosa PA01, section 417 of 529 of the complete genome.' sequence, 16 May 2000.	1-4 -----
Y,P		5-11, 15-17
X,P ---	Database GenBank, US National Library of Medicine, (Bethesda, MD, USA), No. 9950648, STOVER et al. 'UDP-N-acetylmuramoylalanyl-D-glutamyl-2,6-diaminopimelate-- D-alanyl ligase [Pseudomonas aeruginosa].' sequence, 16 May 2000.	8 -----
Y,P		1-7, 9-11, 15-17

☒ Further documents are listed in the continuation of Box C.
 ☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*A* document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*E* earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*G* document member of the same patent family
*O* document referring to an oral disclosure, use, exhibition or other means	
*P* document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

11 DECEMBER 2000

Date of mailing of the international search report

30 JAN 2001

 Name and mailing address of the ISA/US  
 Commissioner of Patents and Trademarks  
 Box PCT  
 Washington, D.C. 20231

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Telephone No. (703) 308-0196



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## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/24437

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X - Y	American Society for Microbiology Abstract, 97th General Meeting, 4-8 May 1997, (Miami Beach, FL, USA), page 318, column 2, the abstract No. H-203, SANSCHAGRIN et al. 'Bacterial genomics and characterization of the cell division/cell-wall biosynthesis locus isolated from a BAC library of <i>Pseudomonas aeruginosa</i> .' Abstracts of the 97th General Meeting for the American Society of Microbiology. 1997, see entire document.	1-4 ----- 5-11, 15-17
X - Y	DEWAR et al. <i>Pseudomonas aeruginosa</i> PA01 Bacterial Artificial Chromosomes: Strategies for Mapping, Screening, and Sequencing 100 kb Loci of the 5.9 Mb Genome. <i>Microbial &amp; Comparative Genomics</i> . 1998, Vol. 3, No. 2, pages 105-117, see entire document.	1-4 ----- 5-11, 15-17
Y	LIAO et al. Cloning and Characterization of the <i>Pseudomonas aeruginosa</i> pbpB Gene Encoding Penicillin-Binding Protein 3. <i>Antimicrobial Agents and Chemotherapy</i> . August 1995. Vol. 39, No. 8, pages 1871-1874, see entire document.	1-11, 15-17
A	IKEDA et al. Homology among murC, murD, murE, and murF Proteins in <i>Escherichia coli</i> and that between <i>E. coli</i> murG and a possible murG Protein in <i>Bacillus subtilis</i> . <i>J. Gen. Appl. Microbiol.</i> 1990, Vol. 36, pages 179-187.	1-11, 15-17



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# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/24437

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:  
1-11, 15-17
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.



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**INTERNATIONAL SEARCH REPORT**

International application No.  
PCT/US00/24437

A. CLASSIFICATION OF SUBJECT MATTER: .  
IPC (7):

C07H 21/02, 21/04; C12N 15/00, 15/09, 15/63, 15/70, 15/74, 9/00, 1/20, 1/14, 1/16, 1/18, 5/04, 5/10, 5/00; G01N 33/53





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